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[Animal models and their results in relation to the therapy of migraine]

[Article in German]

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Until now, our understanding of migraine pathophysiology has been fairly incomplete. So far no animal model has allowed an explanation of all facets of the clinically heterogeneous condition migraine. However, it is now generally accepted that the migraine headache is due to activation of the trigeminal system. The model of neurogenic inflammation after stimulation of the trigeminal ganglion or systemic administration of capsaicin allows study of the inhibitory interactions between antimigraine compounds and peripheral trigeminal fibre terminals that sustain a sterile meningeal inflammation through release of allogenic and vasoactive neuropeptides, such as substance P and calcitonin gene-related peptide. Studies with the model of superior sagittal sinus stimulation have revealed central actions of antimigraine agents such as ergotamine and sumatriptan, but also acetylsalicylic acid on neurotransmission of trigeminal nociceptive input in the brainstem. A likely explanation for the slowly progressing neurological deficits is cortical spreading depression (CSD), which can easily be elicited in many species. However, CSD has not been observed in vivo in humans. The described models strongly influenced the development of new medications for migraine treatment and have improved our understanding of migraine pathophysiology.

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Comment in:

- Cephalalgia. 1996 Apr;16(2):77.

Inhalational anesthetics inhibit spreading depression: relevance to migraine.

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Cortical spreading depression (SD) has not been shown in the human neocortex by direct cortical recordings. However, animal studies suggest that cortical injury, such as that occurring during neurosurgical procedures, should result in the initiation of SD. It is possible that inhibition of SD by volatile anesthetic agents may partially explain the failure to observe SD in the human neocortex during surgery. This study examines the effect of the anesthetic agents alpha-chloralose, halothane, nitrous oxide and isoflurane on the initiation of cortical SD in the cat neocortex. SD was seen in 100% of cats anesthetized with alpha-chloralose ($n = 15$), in 3 of 7 (42%) animals anesthetized with isoflurane ($p < 0.05$, chi 2 with Yates correction) and none of the animals ($n = 4$, 6 hemispheric preparations) anesthetized with halothane ($p < 0.005$, chi 2 with Yates correction, halothane vs alpha-chloralose group). In all cases this inhibitory effect was reversible. In four animals the administration of nitrous oxide (66%) reduced the inspired concentration of isoflurane required to inhibit SD by 0.75%. This study suggests that halothane, and to a lesser extent isoflurane and nitrous oxide, protect against the initiation of cortical SD. This observation may partially explain why SD has not been demonstrated in human neocortex during surgery. Further studies are needed to determine if SD may occur under pathological conditions, such as during migraine with aura, where the cortex may be predisposed to SD.

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